Prostate drug decision highlights urgent need for reform

August 18 2014, by Henry Scowcroft

Just a week after the controversy over breast cancer drug Kadcyla, the inflexibilities within the UK's disparate drug approval systems have been pulled into sharp focus once again.

NICE – the organisation that tells the English and Welsh NHS which drugs it should pay for – has said that the health service should not routinely give prostate cancer drug abiraterone (aka Zytiga), to men whose disease has stopped responding to hormone treatment, before

they've had a course of chemotherapy.

The drug was approved for use after chemo in 2011. Today's decision prevents its routine use earlier in men's treatment.

The reasons for this decision are complex, and relate to the drug's cost, and a disagreement over whether using it before chemotherapy constitutes an 'End of Life' treatment (and thus able to be considered under a more flexible set of criteria) – we'll explore these below in more detail.

But the root cause is a system whose complex incentives ultimately slow down access to treatments that doctors know will benefit their patients – a system we've called on the Government to reform.

Let's look at how this unfortunate situation came to pass.

Prostate cancer, hormones and abiraterone – a brief history

Some prostate cancers are addicts: they depend on male sex hormones like testosterone to grow.

For this reason, men whose cancer has begun to spread (or is likely to spread) are given drugs that lower their testosterone levels. But over time this can stop working, as the cancer starts to make its own hormones.

Until recently, men whose cancer had spread but had become resistant to these hormone therapies had only one treatment option: chemotherapy, which gave them on average three more months.

But after that, if the cancer came back there was nothing their doctor

could do.

But abiraterone offers men a little more time. It was developed by pharmaceutical company Janssen, after Cancer Research UK-funded researchers at The Institute of Cancer Research discovered a molecule that could shut down testosterone production.

In late 2011, Janssen was granted a licence to sell it in the EU to treat these men, after trials showed it could extend their lives by an extra four months on top of the three months from the chemo.

A year later, it was made available use across the NHS for men whose cancer had started growing again after chemotherapy.

But it's not approved to treat men before they've had chemo. And here's where today's decision comes in.

Double the numbers

Each year, according to Cancer Research UK's prostate cancer expert Professor Malcolm Mason, around 11,000 men with advanced prostate cancer are told their hormone treatment has stopped working, and that their cancer will start growing again.

"However, only around half these men go on to have chemotherapy," he told us.

"This is for several reasons. Some choose not to – it can be quite debilitating, and not everyone wants to go through this."

Others, says Prof Mason, aren't suitable – either because of their physical condition, or because they have other illnesses that mean the treatment could carry serious risks.

"So at the moment the number of men for whom NICE says abiraterone is recommended is about 5,000," he says.

End of Life criteria

Abiraterone owes its approval for use after chemo to NICE's 'End of Life' criteria, introduced in 2009 to allow the organisation to be more flexible in paying for drugs:

- for a small population of patients
- who are not expected to live for more than 2 years,
- where the drug could extend their lives by at least 3 months.

This allowed NICE to approve abiraterone, given the data available from clinical trials at the time, and a deal on price from Janssen.

Typically, NICE allows such "End of Life" drugs to be approved below a threshold of about £50,000 per QALY.

We were pleased to see the drug approved as it makes a real difference – and, to be completely transparent here, we do benefit from this decision. Cancer Research UK licensed abiraterone to Janssen, and we receive a small royalty from the drug's sales, which we reinvest in our research.

Using it pre-chemo

Wind forward to January 2013, and a clinical trial called COUGAR-302 showed that giving abiraterone before chemotherapy could be even more beneficial.

The trial hadn't been running long enough to show for certain how much

extra life this would lead to, but it did show that the drug could double the time between the hormone therapy failing and the cancer returning, from about 8 months to around 16.

As a result, NICE was asked to look at whether it would be suitable for use at this earlier point in a man's treatment.

While they looked at the data and talked to Janssen about how best to pay for the drug, men were (and are) still able to get abiraterone on the NHS – in England through a mechanism called the Cancer Drugs Fund, and elsewhere in the UK via something called an Individual Funding Request.

"This has essentially acted as a way to help patients get treatment while the system works out the numbers," says Prof Mason.

A disappointing decision

Today, NICE has made its final decision on earlier use of abiraterone – and it's a no. Why?

"NICE's End of Life criteria have a cut-off point," says Prof Mason "They can only apply for patients who are expected to live for two years or less".

But Prof Mason says the untreated men on the COUGAR triallived for about 30 months, and that's above the threshold for NICE to use 'End of Life' criteria. "Paradoxically, these men are living too long for NICE to approve a drug they could benefit for," he says.

This highlights the inflexibility in the system. "The drug works, but the system's arbitrary built-in cut-off point – coupled to the drug's price – means NICE is obliged to say no, under its own rules." Janssen has

pointed out that the system in Scotland uses a cut-off of 36 months.

NICE has replied that the drug is simply too expensive for the benefit it brings, and wants Janssen to reconsider how it prices it.

What next?

This situation is deeply disappointing and very frustrating for all concerned. Janssen has said it will appeal against it, but it's hard to see how NICE can say 'yes' unless a deal is struck over how to pay for the drug, or unless the two parties can resolve their difference about whether it's an 'End of Life' drug.

We hope this deal can be done – after all, using abiraterone before chemotherapy allows it to be offered to almost double the number of men, and for longer, than it does at the moment. Intuitively, one feels that there has to be a way for Janssen, the NHS, and patients to benefit.

But more than this, it's a situation that shouldn't have been allowed to develop in the first place. The system clearly needs urgent reform, so effective drugs can be approved rapidly, without the need for temporary measures like the Cancer Drugs Fund.

This is especially urgent as more expensive new drugs that target smaller groups of patients come to market.

The Government, the industry, NICE and the NHS have to work this out – sooner rather than later.

Provided by Cancer Research UK